A Randomized, Controlled Phase 3 Study, LIBERTY ASTHMA QUEST, Evaluating the Efficacy and Safety of Dupilumab in Uncontrolled Moderate-to-Severe Asthma

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Rationale: Dupilumab, a fully human anti-interleukin (IL)-4R-α monoclonal antibody that inhibits signaling of IL-4 and IL-13, key drivers of type 2 inflammation, is approved in the EU, USA, Japan, and other countries for treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis (AD). LIBERTY ASTHMA QUEST is a randomized, double-blind, placebo-controlled, parallel group, phase 3 study (NCT02414854) evaluating the efficacy and safety of dupilumab as add-on therapy in patients with uncontrolled, moderate-to-severe asthma. Methods: Patients aged ≥12 years with moderate-to-severe asthma uncontrolled with medium-to-high dose inhaled corticosteroids and up to 2 additional controllers were randomized 2:1 to receive add-on subcutaneous dupilumab in 200 mg or 300 mg doses or matched placebos every 2 weeks (q2w) for 52 weeks. The primary efficacy endpoints of the study were annualized rate of severe exacerbation events over the 52-week treatment period and absolute change from baseline to Week 12 in pre-bronchodilator forced expiratory volume in 1 second (FEV_1). Results: In 1,902 randomized patients, dupilumab 200 mg and 300 mg q2w significantly reduced annualized severe exacerbation rates vs matched placebos by 48% and 46%, respectively (both $P<0.0001$), and improved FEV_1 at Week 12 (least-squares mean difference vs placebo 0.14/0.13 L for 200/300 mg; both $P<0.0001$) in the overall population. Reductions in annualized exacerbation rates vs placebo were 56%/60% for dupilumab 200/300 mg, respectively, in patients with blood eosinophils ≥150 cells/μL; 66%/67% with ≥300 cells/μL; 65%/61% with fractional exhaled nitric oxide (FeNO) ≥25 ppb; and 70%/70% with FeNO ≥50 ppb. FEV_1

improvements vs placebo from baseline to Week 12 were 0.17/0.15 L for dupilumab 200/300 mg in patients with blood eosinophils ≥150 cells/µL; 0.21/0.24 L with ≥300 cells/µL; 0.23/0.24 L with FeNO ≥25 ppb; and 0.30/0.39L with FeNO ≥50 ppb. The most frequent adverse event (AE) occurring more often in the dupilumab 200/300 mg-treated groups compared with the placebo groups was injectionsite reactions (15%/18% vs 5%/10%, respectively). Conjunctivitis AEs were similar between dupilumab and placebo groups, in contrast to dupilumab studies in AD. Conclusions: Dupilumab significantly reduces severe asthma exacerbations and improves lung function, and was generally well tolerated in patients with uncontrolled moderate-to-severe asthma.

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